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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
ANNA BERGGREN, ET AL.	: EXAMINER: PRATT
SERIAL NO: 09/926,586	:
FILED: NOVEMBER 21, 2001	: GROUP ART UNIT: 1761
FOR: NEW COMPOSITION	:

REPLY BRIEF

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

This is in reply to the Examiner's answer mailed September 13, 2005.

There are two fundamental points that the Office has failed to recognize that distinguish the claimed invention from the cited prior art:

(1) the cited prior art fails to provide any disclosure or suggestion for the selection of viable lactobacilli having a positive effect on human intestinal mucosa; and

(2) the cited prior art fails to describe or suggest a sports drink as claimed.

The Examiner does not understand the expression "viable lactobacilli having a positive effect on human intestinal mucosa" and interprets this expression to include many of the known lactobacilli. The Examiner states that claims 15, 25, 36, 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connolly and in view of Kurppa because "Connolly discloses that it is known as in claim 15 to use probiotic bacteria to enhance metabolic processing from the gastrointestinal tract using acidophilus bacteria or other lactic producing bacteria (abstract)" (page 7 of the Examiner's answer).

This interpretation is simply not correct.

The specification at page 3, lines 17-22 states:

> Lactobacilli which are suitable to use in accordance with the invention comprise those different strains of different species which have a positive effect on human intestinal mucosa. Such an effect involves an ability to colonise in the intestines and thereby protect the intestinal mucosa, for instance by initiating the production of mucin or short chain fatty acids.

The Examiner seems to think that it is possible to combine any lactobacilli with anything (such as vitamins, minerals and protein) and still be able to achieve a drinkable sports drink which has a long shelf life and good taste. This is not true. Many lactobacilli are very sensitive to the environment in which they reside and cannot handle an environment at a low pH. The inventors have shown that, for example, *Lactobacillus plantarum* 299v does manage such an environment for up to 4 weeks in a refrigerator. The inventors have further shown that said *Lactobacillus plantarum* 299v have a positive effect on human mucosa and relieving stress symptoms (see "pilot study" on pages 14-15 of the specification).

Connolly's disclosure of "incorporating probiotic bacteria to enhance metabolic processing from the gastrointestinal tract and utilization in the body, and such probiotic organism preferably include bifido bacteria combined with acidophilus bacteria or other lactic acid producing bacteria" is **not** the same thing as having a positive effect on the intestinal mucosa.

Viable lactobacilli having a positive effect on human intestinal mucosa, as claimed, involves an ability to colonise in the intestines and thereby protect the intestinal mucosa by, for example, initiating the production of mucin and/or short chain fatty acids (see p. 3, lines 17-22 of the specification). Intestinal mucin production is an important defence mechanism against pathogens (such as E coli strains EHEC, salmonella etc) by hindering the pathogens from adhering to the intestinal mucosa. Probiotics with ability to adhere to the mucosa which

stimulate production of mucins and hinder *E. coli* from adhering result in an effective probiotic as being healthy for the gut (see again, page 3 of the specification).

Connolly describes adding probiotic bacteria that "choke out" other harmful organisms by "creating metabolic by-products" (see [0032], page 10 of Connolly). Connolly does not describe selecting organisms having any effect on the actual mucosal health (intestinal linings). For optimal effect on the mucosa it is required that a probiotic micro organism binds to it and it is a well known that short-chain fatty acids (SCFA), produced by colonic bacteria are used as an energy substrate of the colonocytes (see, e.g., page 3, 3rd paragraph in the specification). It is of great importance that these beneficial by-products are produced near the mucosa. Connolly, on the other hand, describes that the probiotic micro organisms "help, repair and maintain healthy intestinal linings" by scavenging harmful compounds ([0037], page 3 of Connolly). Thus, it is clear that Connolly provides no suggestion or motivation, alone or when combined with the other cited art, for selecting the bacteria having a positive effect on human intestinal mucosa as set forth by the Inventors in this application and claims.

On page 8 of the Examiner's Answer, the examiner states that nothing has been shown in the prior art that adding lactobacilli to beverages would create a problem. However, the Examiner overlooks some important facts. Since the lactobacilli are viable, the lactobacilli can metabolize the ingredients present in the environment in which it is placed, e.g., a sports drink. The lactobacilli can for instance destroy the active ingredients and produce products giving a bad taste and short shelf-life. The environment effects the lactobacilli present and if the environment is too harsh and/or the lactobacilli too sensitive the lactobacilli die. The prior art simply does not address these problems associated with sports drinks ingested by human consumers.

On page 8 of the Examiner's answer, the examiner states that poor absorption of foods (proteins) can of course make for gastrointestinal disturbances in view of Connolly. However, that statement is made in view of the abnormal high protein diet that a body builder is taking in order to gain muscle tissue (see p. 1, [0004] of Connolly). A normal human being taking a normal dose of protein per day does not have absorption problems of protein or any of the problems relating to a high-protein diet addressed in Connolly.

The particular strains in claims 36 and 37, especially *Lactobacillus plantarum* 299v, have been shown to have the desirable effects of the invention, i.e. viability in a sports drink at low pH and long shelf life without affecting the contents thereof and at the same time relieving stress symptoms.

The claimed sports drink would not have been obvious by combining Connolly with Molin. Again Connolly aims at enhancing protein absorption and utilization from the gastrointestinal tract for use by body builders and Molin to a nutrient composition for administration to patients, especially via a tube, or as a nutrient to horses. There is simply nothing in Mollin which allows one to envision selecting lactobacilli having positive effects on human intestinal mucosa in a sports drink suitable for storage and human consumption.

Further, the probiotic bacteria in Connolly is provided to reach $1x10^5$ to $1x10^8$ counts per gram of skim milk protein concentrate (page 2, [0028] of Connolly). Intake of 200g concentrate per day results in a daily intake of at the most $2x10^7$- $2x10^{10}$ cfu per day.

As set forth in Claim 22, however, the probiotic strain in the sports drink is present in amount of $5x10^7 - 5x10^8$ cfu/ml giving a daily dose of at least $1x10^{10}$ to $1x10^{11}$ cfu--a 10 times higher dose of probiotics.

The main reason for Connolly to add probiotics to the milk protein concentrate is to get a more efficient digestion of eaten foods (especially proteins), less harmful side effects

from consuming large quantities of protein and more efficient utilisation per gram of protein consumed. These are the main objects of the product disclosed by Connolly.

In contrast, the sports drink of the present invention is for a human performing physical activity, the purpose is not to build up muscle tissue, but to build up and recover the energy and fluid levels of the human body before or after physical activity and also relieving the symptoms of stress. This is discussed in the specification on p. 2, last line, and p. 3, lines 1-8. The viable lactobacilli can be mixed with the micronutrients, carbohydrates, salts and proteins, without negative effects on e.g. antioxidants, to a beverage having a good taste and a good shelf life. Since the lactobacilli used in the sports drink of the present invention are viable, it is indeed inventive to find such lactobacilli that are able to survive in the sports drink during the shelf life without affecting taste or the content of other present "active" ingredients. This has been investigated and also mentioned in the examples, see last part of example 1. However, nothing is mentioned in Connolly or any of the other cited prior art about selecting such bacteria with the need for a stable shelf life of the composition.

With respect to Claim 25 to a method of treating stress symptions, gastrointestinal disturbances, and lesions of the mucosal membrane of the intestine, the prior art simply does not describe or suggest the method. Certainly, the prior art does not administer their compositions with the intent of treating such symptoms in the manner as claimed. This is particularly evident based on the fact that the conditions to be treated in claim 25 have not been disclosed in Connolly. The only symptoms to be treated in Connolly are harmful side effects from consuming large quantities of proteins. Further, intake of such large amounts of proteins is only done by body builders, and such conditions cannot be applied to any human performing exercise.

Accordingly, in view of the above in combination with the reasons set forth in Appellants Appeal Brief of August 1, 2005, all of the prior art rejections should be reversed and all pending claims should be indicated as being allowed.

Respectfully submitted,

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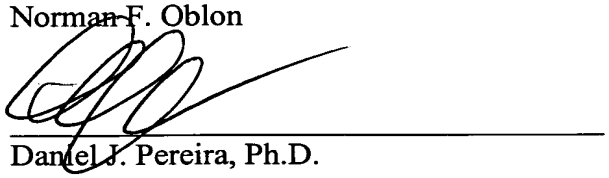

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